

SEQUENCE LISTING

<110> Tanzi, Rudolph E.
Kovacs, Dora
Saunders, Aleister J.

<120> Alpha-2-Macroglobulin Therapies and Drug Screening Methods for
Alzheimer's Disease

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<150> 09/241,606

<151> 1999-02-02

<150> 09/148,503

<151> 1998-09-04

<150> 60/093,297

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Met Gly Leu Lys Ala Phe Thr Asn Ser Lys Ile Arg Lys Pro Lys Met
675 680 685

Cys Pro Gln Leu Gln Gln Tyr Glu Met His Gly Pro Glu Gly Leu Arg
690 695 700

Val Gly Phe Tyr Glu Ser Asp Val Met Gly Arg Gly His Ala Arg Leu
705 710 715 720

Val His Val Glu Glu Pro His Thr Glu Thr Val Arg Lys Tyr Phe Pro
725 730 735

Glu Thr Trp Ile Trp Asp Leu Val Val Val Asn Ser Ala Gly Val Ala
740 745 750

Glu Val Gly Val Thr Val Pro Asp Thr Ile Thr Glu Trp Lys Ala Gly
755 760 765

Ala Phe Cys Leu Ser Glu Asp Ala Gly Leu Gly Ile Ser Ser Thr Ala
770 775 780

Ser Leu Arg Ala Phe Gln Pro Phe Phe Val Glu Leu Thr Met Pro Tyr

785	790	795	800
Ser Val Ile Arg Gly Glu Ala Phe Thr Leu Lys Ala Thr Val Leu Asn			
805	810	815	
Tyr Leu Pro Lys Cys Ile Arg Val Ser Val Gln Leu Glu Ala Ser Pro			
820	825	830	
Ala Phe Leu Ala Val Pro Val Glu Lys Glu Gln Ala Pro His Cys Ile			
835	840	845	
Cys Ala Asn Gly Arg Gln Thr Val Ser Trp Ala Val Thr Pro Lys Ser			
850	855	860	
Leu Gly Asn Val Asn Phe Thr Val Ser Ala Glu Ala Leu Glu Ser Gln			
865	870	875	880
Glu Leu Cys Gly Thr Glu Val Pro Ser Val Pro Glu His Gly Arg Lys			
885	890	895	
Asp Thr Val Ile Lys Pro Leu Leu Val Glu Pro Glu Gly Leu Glu Lys			
900	905	910	
Glu Thr Thr Phe Asn Ser Leu Leu Cys Pro Ser Gly Gly Glu Val Ser			
915	920	925	
Glu Glu Leu Ser Leu Lys Leu Pro Pro Asn Val Val Glu Glu Ser Ala			
930	935	940	
Arg Ala Ser Val Ser Val Leu Gly Asp Ile Leu Gly Ser Ala Met Gln			
945	950	955	960
Asn Thr Gln Asn Leu Leu Gln Met Pro Tyr Gly Cys Gly Glu Gln Asn			
965	970	975	
Met Val Leu Phe Ala Pro Asn Ile Tyr Val Leu Asp Tyr Leu Asn Glu			
980	985	990	
Thr Gln Gln Leu Thr Pro Glu Ile Lys Ser Lys Ala Ile Gly Tyr Leu			
995	1000	1005	

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Leu Thr Ala Gln Pro Ala Pro Thr Ser Glu Asp Leu Thr Ser Ala Thr
1220 1225 1230

Asn Ile Val Lys Trp Ile Thr Lys Gln Gln Asn Ala Gln Gly Gly Phe
1235 1240 1245

Ser Ser Thr Gln Asp Thr Val Val Ala Leu His Ala Leu Ser Lys Tyr
1250 1255 1260

Gly Ala Ala Thr Phe Thr Arg Thr Gly Lys Ala Ala Gln Val Thr Ile
1265 1270 1275 1280

Gln Ser Ser Gly Thr Phe Ser Ser Lys Phe Gln Val Asp Asn Asn Asn
1285 1290 1295

Arg Leu Leu Leu Gln Gln Val Ser Leu Pro Glu Leu Pro Gly Glu Tyr
1300 1305 1310

Ser Met Lys Val Thr Gly Glu Gly Cys Val Tyr Leu Gln Thr Ser Leu
1315 1320 1325

Lys Tyr Asn Ile Leu Pro Glu Lys Glu Glu Phe Pro Phe Ala Leu Gly
1330 1335 1340

Val Gln Thr Leu Pro Gln Thr Cys Asp Glu Pro Lys Ala His Thr Ser
1345 1350 1355 1360

Phe Gln Ile Ser Leu Ser Val Ser Tyr Thr Gly Ser Arg Ser Ala Ser
1365 1370 1375

Asn Met Ala Ile Val Asp Val Lys Met Val Ser Gly Phe Ile Pro Leu
1380 1385 1390

Lys Pro Thr Val Lys Met Leu Glu Arg Ser Asn His Val Ser Arg Thr
1395 1400 1405

Glu Val Ser Ser Asn His Val Leu Ile Tyr Leu Asp Lys Val Ser Asn
1410 1415 1420

Gln Thr Leu Ser Leu Phe Phe Thr Val Leu Gln Asp Val Pro Val Arg
1425 1430 1435 1440

Asp Leu Lys Pro Ala Ile Val Lys Val Tyr Asp Tyr Tyr Glu Thr Asp

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1445

1450

1455

Glu Phe Ala Ile Ala Glu Tyr Asn Ala Pro Cys Ser Lys Asp Leu Gly
1460 1465 1470

Asn Ala

<210> 3

<211> 750

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)..(750)

<223> Aβ/LRP Binding Domain

<400> 3

tcg gag gac ctg acc tct gca acc aac atc gtg aag tgg atc acg aag 48
Ser Glu Asp Leu Thr Ser Ala Thr Asn Ile Val Lys Trp Ile Thr Lys
1 5 10 15

cag cag aat gcc cag ggc ggt ttc tcc tcc acc cag gac aca gtg gtg 96
Gln Gln Asn Ala Gln Gly Gly Phe Ser Ser Thr Gln Asp Thr Val Val
20 25 30

gct ctc cat gct ctg tcc aaa tat gga gcc gcc aca ttt acc agg act 144
Ala Leu His Ala Leu Ser Lys Tyr Gly Ala Ala Thr Phe Thr Arg Thr
35 40 45

ggg aag gct gca cag gtg act atc cag tct tca ggg aca ttt tcc agc 192
Gly Lys Ala Ala Gln Val Thr Ile Gln Ser Ser Gly Thr Phe Ser Ser
50 55 60

aaa ttc caa gtg gac aac aac aat cgc ctg tta ctg cag cag gtc tca 240
Lys Phe Gln Val Asp Asn Asn Asn Arg Leu Leu Leu Gln Gln Val Ser
65 70 75 80

ttg cca gag ctg cct ggg gaa tac agc atg aaa gtg aca gga gaa gga 288
Leu Pro Glu Leu Pro Gly Glu Tyr Ser Met Lys Val Thr Gly Glu Gly

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85

90

95

tgt gtc tac ctc cag acc tcc ttg aaa tac aat att ctc cca gaa aag 336
Cys Val Tyr Leu Gln Thr Ser Leu Lys Tyr Asn Ile Leu Pro Glu Lys
100 105 110

gaa gag ttc ccc ttt gct tta gga gtg cag act ctg cct caa act tgt 384
Glu Glu Phe Pro Phe Ala Leu Gly Val Gln Thr Leu Pro Gln Thr Cys
115 120 125

gat gaa ccc aaa gcc cac acc agc ttc caa atc tcc cta agt gtc agt 432
Asp Glu Pro Lys Ala His Thr Ser Phe Gln Ile Ser Leu Ser Val Ser
130 135 140

tac aca ggg agc cgc tct gcc tcc aac atg gcg atc gtt gat gtg aag 480
Tyr Thr Gly Ser Arg Ser Ala Ser Asn Met Ala Ile Val Asp Val Lys
145 150 155 160

atg gtc tct ggc ttc att ccc ctg aag cca aca gtg aaa atg ctt gaa 528
Met Val Ser Gly Phe Ile Pro Leu Lys Pro Thr Val Lys Met Leu Glu
165 170 175

aga tct aac cat gtg agc cgg aca gaa gtc agc agc aac cat gtc ttg 576
Arg Ser Asn His Val Ser Arg Thr Glu Val Ser Ser Asn His Val Leu
180 185 190

att tac ctt gat aag gtg tca aat cag aca ctg agc ttg ttc ttc acg 624
Ile Tyr Leu Asp Lys Val Ser Asn Gln Thr Leu Ser Leu Phe Phe Thr
195 200 205

gtt ctg caa gat gtc cca gta aga gat ctc aaa cca gcc ata gtg aaa 672
Val Leu Gln Asp Val Pro Val Arg Asp Leu Lys Pro Ala Ile Val Lys
210 215 220

gtc tat gat tac tac gag acg gat gag ttt gca atc gct gag tac aat 720
Val Tyr Asp Tyr Tyr Glu Thr Asp Glu Phe Ala Ile Ala Glu Tyr Asn
225 230 235 240

gct cct tgc agc aaa gat ctt gga aat gct 750
Ala Pro Cys Ser Lys Asp Leu Gly Asn Ala
245 250

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<210> 4
 <211> 250
 <212> PRT
 <213> Homo sapiens

<400> 4

Ser	Glu	Asp	Leu	Thr	Ser	Ala	Thr	Asn	Ile	Val	Lys	Trp	Ile	Thr	Lys
1				5					10					15	
Gln	Gln	Asn	Ala	Gln	Gly	Gly	Phe	Ser	Ser	Thr	Gln	Asp	Thr	Val	Val
			20					25					30		
Ala	Leu	His	Ala	Leu	Ser	Lys	Tyr	Gly	Ala	Ala	Thr	Phe	Thr	Arg	Thr
		35					40					45			
Gly	Lys	Ala	Ala	Gln	Val	Thr	Ile	Gln	Ser	Ser	Gly	Thr	Phe	Ser	Ser
	50					55					60				
Lys	Phe	Gln	Val	Asp	Asn	Asn	Asn	Arg	Leu	Leu	Leu	Gln	Gln	Val	Ser
65					70					75				80	
Leu	Pro	Glu	Leu	Pro	Gly	Glu	Tyr	Ser	Met	Lys	Val	Thr	Gly	Glu	Gly
				85					90					95	
Cys	Val	Tyr	Leu	Gln	Thr	Ser	Leu	Lys	Tyr	Asn	Ile	Leu	Pro	Glu	Lys
			100					105					110		
Glu	Glu	Phe	Pro	Phe	Ala	Leu	Gly	Val	Gln	Thr	Leu	Pro	Gln	Thr	Cys
		115					120					125			
Asp	Glu	Pro	Lys	Ala	His	Thr	Ser	Phe	Gln	Ile	Ser	Leu	Ser	Val	Ser
	130					135					140				
Tyr	Thr	Gly	Ser	Arg	Ser	Ala	Ser	Asn	Met	Ala	Ile	Val	Asp	Val	Lys
145					150				155					160	
Met	Val	Ser	Gly	Phe	Ile	Pro	Leu	Lys	Pro	Thr	Val	Lys	Met	Leu	Glu
				165				170						175	

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Arg Ser Asn His Val Ser Arg Thr Glu Val Ser Ser Asn His Val Leu
 180 185 190

Ile Tyr Leu Asp Lys Val Ser Asn Gln Thr Leu Ser Leu Phe Phe Thr
 195 200 205

Val Leu Gln Asp Val Pro Val Arg Asp Leu Lys Pro Ala Ile Val Lys
 210 215 220

Val Tyr Asp Tyr Tyr Glu Thr Asp Glu Phe Ala Ile Ala Glu Tyr Asn
 225 230 235 240

Ala Pro Cys Ser Lys Asp Leu Gly Asn Ala
 245 250

<210> 5

<211> 333

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)..(333)

<223> Aβ Binding Domain

<400> 5

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 Ser Glu Asp Leu Thr Ser Ala Thr Asn Ile Val Lys Trp Ile Thr Lys
 1 5 10 15

cag cag aat gcc cag ggc ggt ttc tcc tcc acc cag gac aca gtg gtg 96
 Gln Gln Asn Ala Gln Gly Gly Phe Ser Ser Thr Gln Asp Thr Val Val
 20 25 30

gct ctc cat gct ctg tcc aaa tat gga gcc gcc aca ttt acc agg act 144
 Ala Leu His Ala Leu Ser Lys Tyr Gly Ala Ala Thr Phe Thr Arg Thr
 35 40 45

ggg aag gct gca cag gtg act atc cag tct tca ggg aca ttt tcc agc 192
 Gly Lys Ala Ala Gln Val Thr Ile Gln Ser Ser Gly Thr Phe Ser Ser

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50

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60

aaa ttc caa gtg gac aac aac aat cgc ctg tta ctg cag cag gtc tca 240
Lys Phe Gln Val Asp Asn Asn Asn Arg Leu Leu Leu Gln Gln Val Ser
65 70 75 80

ttg cca gag ctg cct ggg gaa tac agc atg aaa gtg aca gga gaa gga 288
Leu Pro Glu Leu Pro Gly Glu Tyr Ser Met Lys Val Thr Gly Glu Gly
85 90 95

tgt gtc tac ctc cag acc tcc ttg aaa tac aat att ctc cca gaa 333
Cys Val Tyr Leu Gln Thr Ser Leu Lys Tyr Asn Ile Leu Pro Glu
100 105 110

<210> 6

<211> 111

<212> PRT

<213> Homo sapiens

<400> 6

Ser Glu Asp Leu Thr Ser Ala Thr Asn Ile Val Lys Trp Ile Thr Lys
1 5 10 15

Gln Gln Asn Ala Gln Gly Gly Phe Ser Ser Thr Gln Asp Thr Val Val
20 25 30

Ala Leu His Ala Leu Ser Lys Tyr Gly Ala Ala Thr Phe Thr Arg Thr
35 40 45

Gly Lys Ala Ala Gln Val Thr Ile Gln Ser Ser Gly Thr Phe Ser Ser
50 55 60

Lys Phe Gln Val Asp Asn Asn Asn Arg Leu Leu Leu Gln Gln Val Ser
65 70 75 80

Leu Pro Glu Leu Pro Gly Glu Tyr Ser Met Lys Val Thr Gly Glu Gly
85 90 95

Cys Val Tyr Leu Gln Thr Ser Leu Lys Tyr Asn Ile Leu Pro Glu
100 105 110

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<210> 7
<211> 417
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> (1)..(417)
<223> LRP Binding Domain

<400> 7
aag gaa gag ttc ccc ttt gct tta gga gtg cag act ctg cct caa act 48
Lys Glu Glu Phe Pro Phe Ala Leu Gly Val Gln Thr Leu Pro Gln Thr
1 5 10 15
tgt gat gaa ccc aaa gcc cac acc agc ttc caa atc tcc cta agt gtc 96
Cys Asp Glu Pro Lys Ala His Thr Ser Phe Gln Ile Ser Leu Ser Val
20 25 30
agt tac aca ggg agc cgc tct gcc tcc aac atg gcg atc gtt gat gtg 144
Ser Tyr Thr Gly Ser Arg Ser Ala Ser Asn Met Ala Ile Val Asp Val
35 40 45
aag atg gtc tct ggc ttc att ccc ctg aag cca aca gtg aaa atg ott 192
Lys Met Val Ser Gly Phe Ile Pro Leu Lys Pro Thr Val Lys Met Leu
50 55 60
gaa aga tct aac cat gtg agc cgg aca gaa gtc agc agc aac cat gtc 240
Glu Arg Ser Asn His Val Ser Arg Thr Glu Val Ser Ser Asn His Val
65 70 75 80
ttg att tac ctt gat aag gtg tca aat cag aca ctg agc ttg ttc ttc 288
Leu Ile Tyr Leu Asp Lys Val Ser Asn Gln Thr Leu Ser Leu Phe Phe
85 90 95
acg gtt ctg caa gat gtc cca gta aga gat ctc aaa cca gcc ata gtg 336
Thr Val Leu Gln Asp Val Pro Val Arg Asp Leu Lys Pro Ala Ile Val
100 105 110

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aat gct cct tgc agc aaa gat ctt gga aat gct 417
Asn Ala Pro Cys Ser Lys Asp Leu Gly Asn Ala
130 135

<400> 8
Lys Glu Glu Phe Pro Phe Ala Leu Gly Val Gln Thr Leu Pro Gln Thr
1 5 10 15

Ser Tyr Thr Gly Ser Arg Ser Ala Ser Asn Met Ala Ile Val Asp Val
35 40 45

Glu Arg Ser Asn His Val Ser Arg Thr Glu Val Ser Ser Asn His Val
65 70 75 80

Thr Val Leu Gln Asp Val Pro Val Arg Asp Leu Lys Pro Ala Ile Val
100 105 110

Asn Ala Pro Cys Ser Lys Asp Leu Gly Asn Ala
130 135

<210> 9
<211> 81
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> (1)..(81)
<223> Consensus LRP Binding Domain

<400> 9
ttc att ccc ctg aag cca aca gtg aaa atg ctt gaa aga tct aac cat 48
Phe Ile Pro Leu Lys Pro Thr Val Lys Met Leu Glu Arg Ser Asn His
1 5 10 15

gtg agc cgg aca gaa gtc agc agc aac cat gtc 81
Val Ser Arg Thr Glu Val Ser Ser Asn His Val
20 25

<210> 10
<211> 27
<212> PRT
<213> Homo sapiens

<400> 10
Phe Ile Pro Leu Lys Pro Thr Val Lys Met Leu Glu Arg Ser Asn His
1 5 10 15

Val Ser Arg Thr Glu Val Ser Ser Asn His Val
20 25

<210> 11
<211> 33
<212> DNA
<213> Homo sapiens

<220>

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<221> CDS

<222> (1)..(33)

<223> Aβ Fibril Inhibitor

<400> 11

cgc gat ctg cca ttc ttc cca gtc cca att gat

33

Arg Asp Leu Pro Phe Phe Pro Val Pro Ile Asp

1

5

10

<210> 12

<211> 11

<212> PRT

<213> Homo sapiens

<400> 12

Arg Asp Leu Pro Phe Phe Pro Val Pro Ile Asp

1

5

10

<210> 13

<211> 114

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)..(114)

<223> Aβ Fibril Inhibitor

<400> 13

cgc gat ctg cca ttc ttc cca gtc cca att gat ttc att ccc ctg aag 48

Arg Asp Leu Pro Phe Phe Pro Val Pro Ile Asp Phe Ile Pro Leu Lys

1

5

10

15

cca aca gtg aaa atg ctt gaa aga tct aac cat gtg agc cgg aca gaa 96

Pro Thr Val Lys Met Leu Glu Arg Ser Asn His Val Ser Arg Thr Glu

20

25

30

gtc agc agc aac cat gtc

114

Val Ser Ser Asn His Val

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<210> 14
<211> 38
<212> PRT
<213> Homo sapiens
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<210> 15
<211> 27
<212> DNA
<213> Homo sapiens
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<400> 15
cgc gat ctg cca ttc ttc cca gtc gat
Arg Asp Leu Pro Phe Phe Pro Val Asp
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<400> 16
Arg Asp Leu Pro Phe Phe Pro Val Asp

1

5

<210> 17
<211> 21
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> (1)..(21)

<400> 17
ctg cca ttc ttc cca gtc gat
Leu Pro Phe Phe Pro Val Asp
1 5

21

<210> 18
<211> 7
<212> PRT
<213> Homo sapiens

<400> 18
Leu Pro Phe Phe Pro Val Asp
1 5

<210> 19
<211> 18
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> (1)..(18)

<400> 19
ctg cca ttc ttc gtc gat
Leu Pro Phe Phe Val Asp
1 5

18

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<210> 20
<211> 6
<212> PRT
<213> Homo sapiens

<400> 20
Leu Pro Phe Phe Val Asp
1 5

<210> 21
<211> 15
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> (1)..(15)

<400> 21
ctg cca ttc ttc gat
Leu Pro Phe Phe Asp
1 5

15

<210> 22
<211> 5
<212> PRT
<213> Homo sapiens

<400> 22
Leu Pro Phe Phe Asp
1 5

<210> 23
<211> 12
<212> DNA
<213> Homo sapiens

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<220>
<221> CDS
<222> (1)..(12)

<400> 23
ctg cca ttc ttc
Leu Pro Phe Phe
1

12

<210> 24
<211> 4
<212> PRT
<213> Homo sapiens

<400> 24
Leu Pro Phe Phe
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<210> 25
<211> 9
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> (1)..(9)

<400> 25
cca ttc ttc
Pro Phe Phe
1

9

<210> 26
<211> 3
<212> PRT
<213> Homo sapiens

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<400> 26

Pro Phe Phe

1

<210> 27

<211> 50

<212> DNA

<213> Homo sapiens

<220>

<223> Noncoding-antisense DNA

<400> 27

catgcaccag gogtgcattg cctcttccca ttacatctga ctctgagtga

50

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